NCRI
National
Cancer
Research
Institute

NCRI Bladder & Renal Cancer Clinical Studies Group

Annual Report 2017-18

Partners in cancer research

NCRI Bladder & Renal Cancer CSG
Annual Report 2017-18

1. Top 3 achievements in the reporting year

Achievement 1

Continued development, leading and delivery of practice changing studies

The CSG-developed POUT trial of peri-operative chemotherapy versus surveillance in completely resected upper tract transitional cell carcinoma (UTUC) closed prematurely on the advice of the IDMC having met its primary endpoint. The study showed a 17% benefit in DFS for adjuvant chemotherapy at two years. POUT was awarded the most practice changing study at the American Society of Clinical Oncology Genitourinary Cancers Symposium (ASCO GU) and won first prize for oncology at the European Association of Urology (EAU) Congress.

Achievement 2

A trial for every patient and ongoing engagement of the urological community with 5413 patients recruited to bladder cancer trials and 376 to renal studies

Many of the recruiting studies in bladder cancer are in non-muscle invasive disease reflecting the greater incidence of that disease. There are new PI's with the DETECT 2 trial and newly opened PROMs based trials in bladder cancer. In advanced disease the ATLANTIS study for post chemotherapy maintenance therapy has opened to 25 sites providing a pragmatic option for a biomarker directed study to a wide proportion of the country. The renal cancer portfolio has significantly expanded directly due to the efforts of the CSG. We have developed and opened studies that will have a major impact on recruitment into RCC clinical trials over the next year. RAMPART (international adjuvant), PRISM (1st line metastatic immunotherapy), EASE (small renal mass), NAXIVA (neoadjuvant), TRACERx and SCOTROCC (translational) are all highly internationally competitive.

Achievement 3

Exemplar consumer engagement and CSG participation in NICE reviews

The Bladder & Renal CSG consumer members continue to provide input par excellence leading a team of patient champions in renal cancer and regional research representatives in bladder cancer. This ensures that all studies in development from the CSG have a robust expert patient

input, supported by clinical mentors. This allows better dissemination of the opportunities provided by going into a trial to patients across the UK, empowering them with the "OK to ask" mantra if a trial is not available to them locally. Both consumer and scientific members of the CSG have contributed to nine National Institute for Health and Care Excellence (NICE) appraisals and a further number of funding submissions. This has helped the success of the NICE reviews where initially unsuccessful applications for new agents were re-evaluated after CSG input. The CSG works jointly with the British Uro-Oncology Group (BUG) to provide joint reports to NICE.

Finally, the CSG has had an increasing number of portfolio adoption applications to review to try and ensure that the research environment does not become overcrowded in niche areas.

2. Structure of the Group

The CSG is made up of 21 members, five clinical oncologists, (all treating with systemic therapies as well as radiation), five medical oncologists, six surgeons, two consumer members and two trainee members. The membership has been substantially refreshed in the reporting year with additional surgical experience in renal and bladder cancer but with a number of core members rotating or due to rotate off the group. The UK pool of research active, experienced and engaged bladder and kidney cancer oncologists and urologists is not exhaustive and it is important that this is taken into account at times of rotation to avoid there being a sudden drop in research activity from the membership. Four bladder specific clinical oncologists and two medical oncologists with RCC expertise have recently stepped down. This required an additional call for clinical oncology bladder specialists in spring 2018. With further planned rotations in Summer 2018 it is important that the CSG secretariat ensure that there is not a gap in bladder or RCC specific input on the Group.

3. CSG & Subgroup strategies

Main CSG

Develop an increased academic portfolio of high quality interventional systemic treatment studies in RCC

The establishment of the Systemic Treatment Working Party has contributed to a major expansion of the RCC trial portfolio with activity in the adjuvant, neo-adjuvant, metastatic and translational settings. RAMPART – a Medical Research Council (MRC) run international randomised phase III study will be open Summer 2018. PRISM, a first line immunotherapy study examining alternative schedule ipilimumab + nivolumab is now open. NAXIVA – a neoadjuvant translational study in patients with IVC tumour thrombus is open and recruiting as is TRACERx which has recently reported in 3 synchronous papers in the highly prestigious journal Cell and continues to generate data. TRIBE, a biomarker study in patients who have received immunotherapy and are moving on to TKI based treatment is open and recruiting. The Systemic Treatments Working Party has proved itself to be an effective generator of studies and will become a formal subgroup of the CSG. Further ideas for studies are in discussion and in various stages of maturity.

Assess the feasibility of a screening programme for early RCC in higher risk individuals

After seeking a wide range of opinion on the optimal strategy for development of screening in RCC (from AAA screening community, primary care experts, National Screening Committee and SPED) it was decided to take a stepwise approach to the development of research into screening for RCC. Mr Grant Stewart (Surgical Subgroup Chair) has led this strand of research. In collaboration with health economists and radiologists at the University of Cambridge three initial research questions are being addressed:

1. What is the predicted cost effectiveness of screening for RCC?
2. Is it feasible to train novices to use ultrasound scanning to identify renal tumours?
3. Can urinary protein biomarkers be used to identify individuals at high risk of harbouring RCC?

These three strands will lead to a pilot study of recruitment to a RCT prior to a full RCT of screening in the optimal population. In tandem, Professor James Catto is developing a screening study for bladder and kidney cancer in individuals with non-visible haematuria, this will provide extra evidence for the development of screening for RCC in a wider cohort of individuals.

Offer as broad a research portfolio as possible through development of high quality competitive trials suitable for every patient

Studies in non-muscle invasive bladder cancer (NMIBC) continue to deliver strongly bringing in new investigators and sites. For example, DETECT 2 has recruited more than three times its

initial sample size allowing strengthening of the power of the study. This study is one that is open in multiple cancer units as well as bigger centres and we need to balance the portfolio to offer these “easy “surgically led studies.
RAMPART, the adjuvant RCC study will be open at most RCC surgical centres across the country. EASE, a small renal mass observational and biopsy study will be deliverable at many surgical units. The RCC portfolio therefore balances pragmatic relatively high-volume studies with lower volume more complex interventional and biomarker studies. PROMs studies are ongoing in single region (Life and bladder and renal cancer) and nationally (Q-ABC trial). The ABSEIL study in NMIBC surveillance has a sample size of 2100 patients and can be offered across units. There are ongoing surgical and radiotherapy studies in radical treatment of MIBC, and neoadjuvant and maintenance studies again in MIBC (NEOBLADE, SPIRE, ATLANTIS).
The practice changing POUT study in Upper tract TCC has completed early, recruiting 261 patients in the UK, and a successor trial is in development. In penile cancer VINCAP achieved its target of 22 patients with an objective response rate of 27% in this rare cancer group and the eagerly awaited InPACT trial run through the rare cancers initiative has now opened.

The CSG continues to face significant competition from industry trials in RCC and metastatic urothelial cancer. This is an opportunity for the CSG to deliver practice changing studies with novel agents both independently of and in collaboration with industry, for example the addition of new arms for the maintenance adaptive platform study ATLANTIS.

Continued liaison with key organisations internationally and nationally

The Bladder & Renal CSG has maintained and grown its links with the British Association of Urological Surgeons (BAUS) and BAUS Section of Oncology, the latter being chaired by Miss Jo Cresswell, former T2 & Below (TABS) Subgroup Chair. BAUS is restructuring its academic section and Mr Grant Stewart is part of this working party. New members have joined the Surgical Subgroup. The Subgroup Chairs will liaise with BAUS Oncology to invite fledgling research active urologists to attend CSG and Subgroup meetings as observers to foster understanding of the work of the CSG and encouraging development of new PI and CIs.

The CSG works closely with the BUG (Dr Alison Birtle is BUG Secretary and Dr Rob Jones is Committee member) allowing joint input on NICE appraisals and wider dissemination of the CSG portfolio, with input from BUG members into trial feasibility. The CSG has initiated development on a non-TCC bladder cancer trial with collaboration internationally through the International Rare Cancers Initiative (IRCI).

The CSG is represented within the SPED Advisory Group by Mr Christopher Blick. Dr Simon Crabb is the chair of the bladder cancer module on the 100,000 Genome Project allowing input into sample use and subsequent generation in biomarker directed clinical studies. Several members of the CSG are involved with the Bladder and Renal Cancer Genomics England Clinical Interpretation Partnership (GeCIPs). The CSG links with the Renal Cross Channel group (UK, France and Italy) which has led to UK involvement with EASE. Increasing links are also being made with the EORTC Renal Cross Channel group. Our RCC consumers link with the International Kidney Cancer Coalition (IKCC).

The CSG must find new ways of engagement with Sub Specialty Leads (SSL) as there has been low uptake on invites to attend CSG meetings and response to CSG newsletters.

Foster new investigators via CSG and subgroups

There are two trainees on the CSG (one trainee is held jointly with BUG. One of the trainees, Dr Sally Appleyard has progressed the Q-ABC study through a number of funding submissions through to a final successful funding and portfolio adoption and has been an active member of the TABS Subgroup. There are a number of studies in portfolio run through the ICR-CTSU and working with the ICR-CTSU and BURST, these trials have appointed a trainee/junior consultant member to each of the Trial Management Groups of these bladder cancer studies to allow urologists in particular exposure to CI or sub-investigator input to an academic study.

Engage new investigators by offering pragmatic studies to run in cancer units balancing biomarker directed systemic studies

In response to the 2013 survey of UK urologists on barriers to recruitment, we must continue to offer studies that can be run in small centres. This started in previous years with the NMIBC trials of BOXIT, DETECT and HYMN, and has continued with CALIBER and DETECT 2 in bladder cancer. ABSEIL is a bladder cancer surveillance study which is due to open and will recruit over 2000 patients. In advanced bladder cancer, the ATLANTIS trial allows for a relatively pragmatic trial that incorporates biomarker selection for novel therapeutics. In renal cancer the theme continues with the small renal cancer surveillance study (EASE) and imminent opening of the UK led academic adjuvant trial RAMPART. If our pilot activity on screening for RCC and bladder cancer is successful, large scale evaluation will involve many centres and new investigators.

Ensure consumer engagement is paramount

The “No decision about me, without me” and “Ok to ask” campaigns underpin the Bladder & Renal CSG passion for consumer engagement from trial concept to trial delivery. Only with this model can we ensure that we develop studies that patients want to be in, look at what the key questions are for patients not just for researchers, to ensure trials can recruit and deliver successfully. The current consumer members of the CSG are internationally known advocates for bladder and renal cancer and it is paramount that new consumer members to the CSG have a cross over period of mentoring. Mrs Rose Woodward, founder of Kidney Cancer Support Network has rotated off the CSG and has agreed to mentor new appointees. Together with Mr Andrew Winterbottom, founder of Fight Bladder Cancer, they have empowered patients to challenge clinicians where studies are not available locally and ask for cross referral.

Highlight areas of unmet need

The CSG has identified investigation of novel combinations of radiotherapy with new systemic agents including immunotherapy as an area of unmet need that requires academically led studies and have established a Combination Radiotherapy/Drug (CIRT) Working Party (led by Dr Vincent Koo) to develop studies in this space. We have identified node positive bladder cancer as an area of unmet need and had developed a study working with Industry for this patient group. Although funding was formally secured from industry, a change in the management structure at the industry partner resulted in the funding being withdrawn due to a change in internal priorities. The CSG continue to approach other partners to secure a successful trial for this area.

Non TCC bladder cancer is usually excluded from most clinical protocols and thus working with Professor Gareth Griffiths from the Supportive & Palliative Care CSG, a proposal has been submitted through the IRCI for a non TCC protocol, working collaboratively with the ANZUP Group and Canadian collaborators among others.

Utilise tissue biorepository

Work has begun on the samples collected during the BCON and BC2001 trials looking at makers of radiation sensitivity and hypoxia modification with a successful Cancer Research UK (CRUK) grant application in the last year to fund this work.

All trials have a tissue collection part and analysis of previous trials has helped inform successor studies e.g. LAMB bio-repository informed ATLANTIS biomarker development for two of its current arms.

The POUT trial translational sub-study, POUT-T, had its funding rescinded prematurely by CRUK, disappointingly given the subsequent positive results of the main trial, work is ongoing to secure further funding for this important tissue set analysis.

TRACERx has generated rich data regarding RCC pathogenesis, heterogeneity and evolution culminating in 3 synchronous papers in Cell (April 2018) with more to come.

Advanced Bladder Cancer Subgroup (Chair, Dr Simon Crabb outgoing chair)

Optimise systemic therapy by developing new drug hypotheses to test in MIBC

In the last year the Advanced Bladder Cancer Subgroup has overseen the addition of a third arm (rucaparib in an HRD biomarker positive subset) to the two original proposed arms (cabozantinib/biomarker negative and enzalutamide/AR positive) within the ATLANTIS platform study. This is the first randomised trial in urothelial cancer to address the question of PARP inhibitor efficacy. We are also developing a study for the addition of immunotherapy for node positive (N0 M0) bladder cancer, a disease setting in which no prospective trials have yet been undertaken. We are also developing a non-TCC study proposal, through IRCI, to attempt to address treatment options for this rare disease subgroup in which the UK academic community have undertaken the only prior dedicated prospective clinical trial. Other options being developed through the Subgroup include a proposal for a BET inhibitor trial, based on evidence for an epigenetic component in the biology of this disease, and two immunotherapy/radiotherapy combination studies I collaboration with pharma.

Deliver potentially practice changing studies

We do not consider that there is an immediate question to take to a phase III study at this stage. Our approach therefore is to develop phase II signal seeking questions with biomarker selection hypotheses as the primary approach to practice changing studies in the future. The main vehicle for this is the ATLANTIS trial which is testing 3 drug/biomarker questions

currently and which will allow for rapid translation to phase III if a positive result is established. In exploring options for new arms, the trial is now able to benefit from the rapid route to clinical testing that its adaptive design affords and this has facilitated ongoing discussions with potential pharma partners where we are now able to offer specific evidence for biomarker performance in samples emerging from ATLANTIS and the prior trial LaMB.

Develop larger translational research programmes

The ATLANTIS study is our main example of execution of a translational research question with three biomarker/drug questions ongoing. We are currently receiving data on a ~400 gene Foundation Medicine panel in recruits to this study providing a mechanism for translational insight into the disease to attract pharma collaborators for new questions to be entered into the trial. The 100,000 Genomes Project is collecting samples from advanced disease patients and we will look to link this to trial entry prospectively with data now becoming available for analysis form Genomics England and with work being led by CSG members.

Penile Subgroup (Chair, Dr Amit Bahl outgoing chair)

Increase engagement in clinical trials through promotion of clinical trials and regular engagement with supraregional teams

The Penile Subgroup has been under the successful chairmanship of Dr Amit Bahl over the past 6 years. This culminated in a most productive year in 2017-2018 with the completion of several clinical studies, opening of a randomised phase III trial and development of several potential studies.

Hold regular six-monthly meeting with the opportunity of joining in person or by teleconference

The Penile Subgroup have been successful in holding regular teleconferences which encourages continued momentum.

Provide recruitment into InpacT and develop further trials

Following IRCI, a randomised Phase III International Penile Advanced Cancer Trial (InPACT) was activated in May 2017 with Dr Steve Nicholson as CI. This complex and ambitious trial has started slowly with 6 cases being recruited from 4 centres in the UK and USA. Much work continues to activate more centres locally and to open the trial worldwide in European mainland, Canada and Australia. Other on-going studies include the single centre study assessing the feasibility of Sentimag®/Sienna+® injection for detecting Inguinal Sentinel Node involvement in penile cancer compared to standard of care radioactive nanocolloid (SentiPen) with Mr Vijay Sangar. Another clinical study with Mr Sangar is a randomised controlled phase II trial assessing the efficacy of low-intensity shock wave therapy post inguinal lymph node dissection to lower surgical complications. This study is being resubmitted following reviewer's comments. There is also development of a new targeted or immunotherapy systemic agent in combination with RT for penile cancer that is on-going with

new pipeline drugs from several pharma companies (Dr Bahl). Assessment of male penile quality of life questionnaires are being development for evaluation.

A multi-centre Phase II trial of Vinflunine chemotherapy in locally-advanced and metastatic carcinoma of the penis (VinCaP) was completed under Dr Lisa Pickering. This study met its primary endpoint and reported a clinical benefit rate (CBR) of 45.5% and was selected for oral presentation at ASCO GU in February 2018 and poster presentation for ASCO in June 2018. The multi-centre JAVA-P study closed following recruitment of 9 cases following lack of response on planned futility analysis. The single centre study evaluating the use of MRI-PET pre-inguinal surgery (Mr Asif Muneer) has 2 arms: the impalpable arm has completed recruitment (N= 46) and recruitment is extended for palpable arm (N= 26).

Provide opportunities for advice and support of application for grants

This is encouraged within the team members with liaison with the regional groups. A formalised structure will be developed for 2019.

Ensure consumer involvement in all projects

This is actively pursued for the Subgroup and all project proposals. The aim is to increase consumer involvement to at least 2.

Ensure trainee involvement in the Subgroup to promote development of future researchers

This will be a focus for 2019.

Surgical Subgroup (Chair, Mr Grant Stewart)

Engage with BAUS and BAUS Oncology on promotion of their new trials

Following repeated discussion with BAUS about the importance of greater engagement with the CSGs to enhance the profile of clinical trials in general amongst urologists there has been a recent driver for greater engagement between BAUS and relevant research stake-holders. Mr Stewart is part of a steering group working with BAUS academic section (led by Mr John McGrath) to redesign the way that BAUS interacts with those agencies involved in clinical trials. It was clear to the BAUS team that the CSGs are key groups for them to work closely with. It is hoped that this initiative will lead to higher profile of clinical trial research, individual clinical trials within BAUS and the development of new PIs and CIs.

Deliver and complete feasibility studies in contentious areas to prove recruitment can be achieved

This aim is being actively addressed by the NAXIVA trial of neoadjuvant axitinib in patients having nephrectomy and IVC tumour thrombectomy a relatively rare patient cohort and one with wide ranging expert opinion on the place of clinical trials. NAXIVA is recruiting ahead of

schedule with excellent engagement from urologists and oncologists working as a team in each of the 4 units open to the study so far, 7 units will open in total. If NAXIVA continues to recruit well a follow-on study will be considered. A further feasibility study in development is around feasibility of recruitment to a RCT of ablation vs surgery of small renal masses, this is led by Dr Maxine Tran and will be undertaken at the Royal Free Hospital, the UKs largest renal cancer unit to determine if this recruitment can be achieved, as it has failed in a previous nationwide clinical trial.

The active surveillance of small renal cancer study (EASE) will shortly open (led by Mr Blick and Mr Stephen Bromage). The UK is leading the drive for a translational element of this European study (led by Mr Stewart and Dr Samra Turajlic). This is a study that has failed to recruit in continental Europe due to challenges obtaining diagnostic biopsies, we do not anticipate this issue in UK.

Liaise with oncologists for neoadjuvant trials

Other than NAXIVA, further neoadjuvant and window-of-opportunity studies are being evaluated in conjunction with oncologists and interventional radiologists. Mr Stewart is developing an adaptive, biomarker endpoint WoO study using novel combinations of systemic therapies (WIRE study). Professor David Nicol and Mr Stewart are developing the RAVE study of TKI loaded embolization beads for selective embolization of patients with locally advanced RCC prior to surgery with the aim of assessing the immune stimulation following this process, to determine if use in conjunction with adjuvant IO agents in the future would be synergistic.

T2 & Below (TABS) Subgroup (Chair, Professor Robert Huddart outgoing chair)

Enhance the outcomes of patients with high risk NMIBC

High risk NMIBC makes up approx. 25% of all bladder cancers is a heterogeneous disease and reliable molecular markers to facilitate targeted/ personalised treatment is highly desirable. During this year, there have been no trials explored in this area, however, it is hoped that data from the genomic programme will help inform further research in this area and it is an area of strategic importance for us.

In early 2018, the multicentre RCTs PHOTO and HIVEC II successfully completed recruitment and follow up is ongoing. These trials will inform treatment options in patients with intermediate and high risk NMIBC (making up approx. 50% of all bladder cancer patients).

Radical surgery – The BRAVO feasibility continues to recruit into a study (funded by Yorkshire Cancer Research) based in Sheffield & Leeds to determine the feasibility of recruitment into an important randomised trial comparing early radical surgery and BCG.

Adjuvant treatment – with the potential of a further global BCG shortage (already experienced on 2 previous occasions), the Subgroup explored the HIVEC III trial (Heated Mitomycin C v BCG) through a HTA proposal, which unfortunately failed to receive support or funding. Taking the

feedback into account, the chief investigator and team, with the support or advice from the subgroup, are pursuing a revised protocol and funding from industry.

Develop improves bladder sparing approaches in muscle invasive bladder disease

A Bladder and Radiotherapy Workshop was held in January 2018 and was well attended.

The multicentre RAIDER trial, exploring more effective and optimal radical radiotherapy as a bladder sparring approach in patients with MIBC, is recruiting very well.

TUXEDO 2, a trial of radiotherapy +/- concomitant and adjuvant Durvulumab has recently received funding from industry.

Neo-adjuvant chemotherapy has become standard of care in fit patients with muscle invasive bladder cancer prior to radical surgery (or radiotherapy) – however, as not every patient will respond to the chemotherapy there is a need to tailor treatment by predicting chemotherapy responders. A recent proposal, supported by the Subgroup, is being developed exploring the use of genomics for this purpose.

Work with the Systemic Treatments Renal Cancer Working Party Strategy to improve neo-adjuvant, concomitant and adjuvant therapies for patients with MIBC

This section also includes work in collaboration with the Advanced Bladder Cancer Subgroup.

The recently completed and highly influential POUT trial in an uncommon subgroup (upper tract urothelial carcinoma) was seen to be a good example of surgical-oncological collaboration. Several lessons were learnt from this trial, including the importance of personal engagement and the use of screening logs – the TABS Subgroup certainly intend to incorporate this best practice in all future developments.

NEOBLADE, a trial of neoadjuvant treatment (comparison between chemotherapy alone and combination of chemotherapy with the Tyrosine Kinase Inhibitor, Nintedanib) developed in partnership with industry, has been recruiting well.

Immuno-oncology (I/O) has been embraced into several recent clinical trials being development for advanced and muscle invasive bladder cancer and is expected to extend into the management of high grade NMIBC in the future.

A trial using radiotherapy comparing radiotherapy alone and combination with Durvalumab, developed and lead by a CSG member with CSG support, has recently received funding from industry.

Seek to understand better and then improve, factors that impact on patient quality of life and experience of bladder cancer treatment

As low grade non-invasive bladder cancers affect 50% of all bladder cancer patients and often remain on long-term cystoscopic surveillance, there is a need to explore new strategies to reduce cost and improve efficiency. The recent NICE recommendation of ceasing surveillance after just 12 months (as opposed to 5 years) in the low risk patient group has been met with a compliance of only 40% (BAUS survey). Consequently, members of the Subgroup have formed

a working group to explore a study utilising QoL/PROMS with incorporation of health economics and primary care input.

Exploring novel biomarkers to potentially replace The AmpseqUR (Amplicon deep sequencing of Urinary DNA) study funded by CRUK has completed 12 months of evaluating free DNA in urine samples initially from Birmingham (BCPP) samples and will soon move to validate the findings utilising samples from the PHOTO trial. A clinical trial development is expected to be the next step.

The Q-ABC study is a good example of trial development by a trainee member with support from the CSG. This study evaluating patient quality of life following treatment for muscle invasive bladder cancer has now received funding and will begin recruitment in the summer of 2018.

The Life and Bladder Cancer study evaluating PROMs in bladder cancer patients from Yorkshire, (supported by Yorkshire Cancer Research) has seen good recruitment, however, collection of data is awaiting regulatory approvals from ODR, DARS and iGUARD.

4. Task groups/Working parties

Remit of Combination Radiotherapy/Drug Working Party

The Combined Modality Therapy using Immunotherapy & Radiotherapy (CIRT) Working Party was setup to outline current opportunities with combined modality therapy using immunotherapy and radiotherapy (RT) in bladder cancer and Renal Cell Cancer (RCC) with the aim of developing develop potential combined modality therapy studies for any treatment landscape gaps in the current portfolio maps for the Bladder & Renal CSG.

Progress to date

In bladder cancer, there existed several current prospective phase I studies in single centres. At the Christie Hospital under Dr Ananya Choudhury, there is an on-going Phase 1a/b dose escalation study with an Anti-PDL1 agent (Durvalumab) in collaboration with Astra Zeneca. This study in metastatic bladder cancer is evaluating 3 different fractionated RT dose regimes of 8Gy, 21 Gy and 36Gy. At the Royal Marsden Hospital under Professor Robert Huddart, a Phase I Study of Hypofractionated RT and Anti-PD1 Antibody (Pembrolizumab) in the treatment of advanced BC is being redesigned following development of dose limiting toxicity at level 1. Nick James has organised a re-development of the BC2001 randomised trial by adding Durvalumab to RT/5FU/MMC in muscle invasive bladder cancer alongside an adjuvant arm. This study is in development. Subsequently a UK workshop was held in February 2018 looking at developing an umbrella study in localised muscle invasive bladder cancer using chemo-RT with hypoxia biomarker lead randomisation using and dose escalation.

In RCC, a randomised Phase II trial proposal by Vincent Khoo to evaluate the Current management Or Radiotherapy ablation in Extracranial oligometastatic disease in RENal cancer managed with Numerous Options (CORE-RENO) was outlined. This was refined through the CIRT, Surgical and Systemic groups into a revised randomised Phase II study proposal Evaluating the Use of Ablative Therapy to current management for Oligometastatic disease in RCC (EqUATOR). In this revised version, the experimental arm could include any ablative therapy compared to RT ablation alone. This trial has the support of the Bladder & Renal CSG aim to canvass wider UK support followed by application development for trial funding.

During the past year, the CIRT Working Party overlapped with several of the existing subgroups within the Bladder and Renal CSG. At a recent last CSG meeting, it was decided that the bladder RT studies will fall within the remit of the Systemic Treatments Working Party whilst the EqUATOR trial proposal will be under the Surgical Subgroup.

Remit of Systemic Treatments Working Party

The Working Party was established to focus on generating a novel internationally competitive portfolio of systemic treatment interventions. At the time of the Working Party establishment, recruitment to RCC trials was low and the highest recruiting study, STAR, was drawing to a close. At the last CSG meeting it was agreed that the Working Party should become a Subgroup reflecting the importance to the CSG and the success of its activity.

Progress to date

The Working Party have together worked hard to increase the level of clinical trial activity across the renal portfolio. Regular engagement (by monthly TC), in a supportive and inclusive environment, has helped to maintain momentum and energy in taking ideas forward. Our aim is to have studies for all patients across the treatment landscape, spanning the neo-adjuvant, adjuvant and metastatic setting, including patients with non-clear cell RCC, and incorporating translational elements wherever possible.

Two studies, developed through the Working Party, have opened to recruitment in 2018. PRISM (CI Dr Naveen Vasudev; BMS funded) is an interventional front-line PII multi-centre study in the metastatic setting, exploring alternative scheduling of combination immunotherapy and with a translational arm. TRIBE (CI Dr Fiona Thistlethwaite; Novartis funded) is a biomarker-driven translational study, examining immunological signatures in patients following disease progression on first-line TKI. Other studies within the renal portfolio include: CALYPSO (CI Professor Thomas Powles), a second-line metastatic trial of immunotherapy +/- a MET inhibitor that is open to recruitment and SUNNIFORECAST (UK CI Dr Ekaterini Boleti), expected to open soon in the UK as a front-line immunotherapy trial for patients with non-clear cell RCC. The role of PET-CT as a biomarker for early response is being investigated in patients treated with nivolumab in a pilot single centre study (CI Dr Charnley).

Moving forwards, as systemic treatment options for patients with renal cancer continue to rapidly evolve, our strategy is to identify key emerging knowledge gaps such as establishing a standard of care post first-line immunotherapy, to continue to work closely with industry and capitalise on the positive engagement we have had to date, to develop an early phase pipeline through the phase I interest of Dr Thistlethwaite and to continue to nurture and support all members in developing study ideas, which remains an explicit stated expectation.

5. Funding applications in last year

This is a challenging environment for our CSG, in particular for bladder cancer which currently receives 0.6% of research spend whilst being the most expensive tumour to treat. Studies developed by the CSG with strong research questions and with patient support, in both large sample size (SURVEY) and niche areas of unmet need (Durva and Treme study, Jones et al) have been unsuccessful. In addition, the HIVEC 3 trial in MNIBC was unsuccessful at HTA as there was concern about only one device manufacturer, a caveat that does not apply to drug studies. The CSG works to ensure submissions in which it has been involved have robust research questions, which patients have also deemed important, and cannot do more, where consulted to improve on this. There continue to be studies submitted for funding which have not been seen or inputted into by the CSG.

Table 2 Funding submissions in the reporting year

Cancer Research UK Clinical Research Committee (CRUK CRC)				
Study	**Application type**	**CI**	**Outcome**	**Level of CSG input**
May 2017				
SURVEY: A Prospective Observational Study to Determine if the UroMark assay, a novel multiplex PCR urine based assay, can Detect Bladder Cancer Recurrence in Patients undergoing Surveillance Cystoscopy	Full application	Professor John Kelly	Not supported	Presented to the CSG shortly before submission and discussed in detail with minimal input into proposal. However fully supported by CSG with strong level of support from scientific and consumer members of panel as potential alternative to invasive method of surveillance for urothelial cancer.
WiZrrD: An adaptive, two-stage single arm phase IB/II biomarker trial assessing the efficacy of the WEE 1 inhibitor AZD1775 in patients with	Full application	Dr Sarah Blagden	Not supported	CSG was not consulted for trial development but were informed of finalised protocol and asked to endorse.

metastatic recurrent renal cancer selected by H3K36me3 expression				Applicants invited for discussion.
November 2017				
Durvalumab + Tremelimumab after Radical Radiotherapy in Lymph Node Positive Urothelial Cancer of the Bladder	Early Phase & Feasibility Study (Full Application)	Professor Robert Jones	Not Supported	CSG discussed and developed in subgroup. Supported by CRUK for endorsement but pharma sponsor withdrew
Validation of a biomarker for selecting radiotherapy combinations for muscle invasive bladder cancer patients	Biomarker Project Award (Full Application)	Professor Catharine West	Supported	CSG discussed and supported
Other committees				
Study	**Committee & application type**	**CI**	**Outcome**	**Level of CSG input**
HIVEC 3	HTA Full application	Dr Jo Cresswell	Not supported	Developed through subgroup. Concern from CSG that feedback was negative about single source of device manufacturer when this does not apply for industry sponsored drug trials.
HYBRID 3	RfPB	Professor Robert Huddart	Not supported	Developed through TABS subgroup
Q-ABC	Fight Bladder Cancer	Dr Sally Appleyard	Supported	Developed through TABS subgroup

6. Consumer involvement

Andrew Winterbottom

Please note that this section has not been received

Rose Woodward

Please note that this section has not been received

7. Priorities and challenges for the forthcoming year

Priority 1 Offer trials across portfolio, including new areas of surveillance and cystoscopic alternatives in NMIBC, surveillance of small renal masses, and adjuvant therapy in RCC engaging with new sites and investigators in cancer units. Publicise trials in bladder and renal cancer through patient championship programme empowering patients to ask for trial entry where not locally available. Work with international groups to co-develop studies and with national groups to encourage new investigators and centres.
Priority 2 Tissue collection and use of bio repository continues to be both a priority and a challenge. The CSG works with the 100,000 Genome Project bladder cancer module and in addition has tissue collection embedded into its recruiting studies. We need to evaluate how best to use this resource. Work is already underway on analysis of BC2001 subsets and work from LAMB trial continues to inform development of new arms of ATLANTIS trial.
Priority 3 To support and develop new investigators in the early stages of their career to engage with the research environment. To ensure guidance from experienced investigators is accessed by young investigators. To maximise the use of the contacts and relationships that experienced investigators have nurtured within industry and academia for the benefit and nurture of young investigators.
Challenge 1 Bladder cancer is experiencing a significant increase in pharma activity, something that the RCC community has experienced for a number of years. This creates opportunity in the form of a greater number of investigational agents of interest in the research environment. However, there is an associated threat from pharma sponsored studies that may directly compete with academic studies. The time taken for academic or alliance studies to secure funding and governance approval means that often Trusts in large volume centres have already opened commercial trials directly competing with CSG developed trials. Whilst this may be a good thing for patients, it directly impacts CSG activity. Similarly, in renal cancer, there are a number of commercial adjuvant studies and the CSG must ensure that its flagship trial RAMPART is supported by centres. Finally, funding success for our academic trial remains low and, whilst this may reflect a more challenging funding environment the CSG needs to work to ensure that

our proposed studies are as competitive as possible. We believe that our reinvigorated membership is well placed to do this.

Challenge 2

Engagement with SSLs and Clinical Research Network (CRN). The CSG have held one event to which SSLs were invited but the turnout was disappointing. In addition, after each CSG, a newsletter summarising key points from the CSG and specific questions regarding new trials in development have been circulated to the SSLs and CRN, Response to these has been extremely poor. The Urology SSLs unlike other SSLs, cover five tumour types and thus liaise with three different CSGs. This may in part account for difficulties in terms of lack of time. The increasing demands from NHS institutions and cut back to study leave affect ability to attend meetings; the CSG has invited SSLs to attend CSG meetings but this has not proved successful. We need to look at other ways to engage such as quarterly skype updates by co-chairs with SSLs and better use of the RDM to, liaise with not only the SSLs but key individuals in each CRN.

Challenge 3

Use of biorepository material and delivering high quality translational studies

This has already begun in the BC2001, BCON and LAMB studies, and each trial in the portfolio has a tissue collection element. Withdrawal of funding from the POUT-T translational study which would have allowed a platform through which to develop liquid biopsy/ctDNA based personalised genomic biomarkers was a major disappointment especially in the context of a positive main study result. An alternative funding mechanism for this will be sought. Learning from the successful TRACERx program will be essential.

8. Appendices

Appendix 1 - Membership of main CSG and subgroups

Appendix 2 – CSG and Subgroup strategies

- A – Main CSG Strategy
- B – Advanced Bladder Cancer Subgroup Strategy
- C – Penile Subgroup Strategy
- D – Surgical Subgroup Strategy
- E – T2 & Below Subgroup Strategy

Appendix 3 - Portfolio Maps

Appendix 4 – Top 5 publications in reporting year

Appendix 5 – Recruitment to the NIHR portfolio in the reporting year

Dr Alison Birtle & Dr Paul Nathan (Bladder & Renal Cancer CSG Co-Chairs)

Appendix 1

Membership of the Bladder & Renal CSG

Name	Specialism	Location
Dr Amit Bahl	Clinical Oncologist	Bristol
Dr Alison Birtle (Co-Chair)	Clinical Oncologist	Preston
Dr Kate Fife	Clinical Oncologist	Cambridge
Professor Robert Huddart	Clinical Oncologist	London
Dr Vincent Khoo	Clinical Oncologist	London
Dr Yvonne Rimmer	Clinical Oncologist	Cambridge
Dr Henry Däbritz*	Clinical Research Scientist	Glasgow
Mr Andrew Winterbottom	Consumer	High Wycombe
Mrs Rose Woodward	Consumer	Truro
Professor Janet Brown	Medical Oncologist	Sheffield
Dr Robert Jones	Medical Oncologist	Glasgow
Dr Paul Nathan (Co-Chair)	Medical Oncologist	Middlesex
Dr Fiona Thistlethwaite	Medical Oncologist	Manchester
Dr Naveen Vasudev	Medical Oncologist	Leeds
Ms Kristina Duggleby	NIHR Cancer Research Network Manager	London
Dr Jane Belfield	Radiologist	Liverpool
Professor Emma Hall	Statistician	London
Mr Christopher Blick	Surgeon	Oxford
Professor James Catto	Surgeon	Sheffield
Mr Mark Johnson	Surgeon	Newcastle
Mr Param Mariappan	Surgeon	Edinburgh
Professor David Nicol	Surgeon	London
Mr Grant Stewart	Surgeon	Cambridge
Dr Sally Appleyard*	Specialist Registrar Clinical Oncology	Sussex

* denotes trainee member

Membership of the Subgroups

Advanced Bladder Cancer Subgroup		
Name	**Specialism**	**Location**
Dr Maria de Santis	Associate Clinical Professor	Warwick
Dr Ananya Choudhury	Clinical Oncologist	Manchester
Dr Alison Birtle	Clinical Oncologist	Preston
Professor Robert Huddart	Clinical Oncologist	London
Dr Sundar Santhanam	Clinical Oncologist	Nottingham
Mr Andrew Winterbottom	Consumer	High Wycombe
Professor John Chester	Medical Oncologist	Cardiff
Dr Simon Crabb (Outgoing Chair)	Medical Oncologist	Southampton
Dr Syed Hussain (Incoming Chair)	Medical Oncologist	Plymouth
Dr Robert Jones	Medical Oncologist	Glasgow
Professor Thomas Powles	Medical Oncologist	London
Professor Maggie Knowles**	Pathologist	Leeds
Professor Gareth Griffiths	Statistician	Southampton

Penile Subgroup		
Name	**Specialism**	**Location**
Dr Amit Bahl (Outgoing Chair)	Clinical Oncologist	Bristol
Dr Jim Barber	Clinical Oncologist	Cardiff
Dr Tony Elliot	Clinical Oncologist	Manchester
Dr Vincent Khoo (Incoming Chair)	Clinical Oncologist	London
Dr Anita Mitra**	Clinical Oncologist	London
Dr Heather Payne**	Clinical Oncologist	London
Mr Neil Walker	Consumer	Bristol
Dr Steve Nicholson**	Medical Oncologist	London
Dr Lisa Pickering**	Medical Oncologist	London
Mark Callaway	Radiologist	Bristol
Dr Miles Walkden**	Radiologist	London
Ms Clare Cruickshank**	Statistician	London
Professor Emma Hall	Statistician	London
Mr Pradeep Bose**	Surgeon	Swansea
Mr David Dickerson**	Surgeon	Somerset
Mr Asaf Muneer	Surgeon	London
Mr Matthew Perry**	Surgeon	London
Mr Vijay Sangar	Surgeon	Manchester
Mr Duncan Summerton	Surgeon	Leicester
Dr Nick Watkin**	Surgeon	London
Mr Roland Donat**	Urologist	Edinburgh
Mr Aditya Manjunath**	Urologist	Bristol
Mr Suks Minhas**	Urologist	London
Dr Cathy Corbishley**	Uropathologist	London

Ms Stephanie Burnett **		London
Mr Wayne Lam**		

Surgical Subgroup		
Name	**Specialism**	**Location**
Mrs Rose Woodward	Consumer	Truro
Mr Christopher Blick	Surgeon	Oxford
Mr Stephen Bromage	Surgeon	Manchester
Mr Tobias Klatte	Surgeon	Bournemouth
Mr Tom Mitchell	Surgeon	Cambridge
Mr Pieter Le Roux	Surgeon	London
Professor David Nicol	Surgeon	London
Mr Grenville Oades	Surgeon	Glasgow
Miss Maxine Tran	Surgeon	London
Mr Grant Stewart (Chair)	Surgeon	Cambridge
Mr Mark Sullivan	Surgeon	Oxford
Mr Ravi Barod	Surgeon	London
Mr Satish Maddineni	Surgeon	Manchester
Mr Alex Laird	Surgeon	Edinburgh
Dr Kate Fife	Clinical oncologist	Cambridge
Dr Vincent Khoo	Clinical oncologist	London
Mr Simon Williams	Surgeon	Derby

T2 & Below Subgroup		
Name	**Specialism**	**Location**
Dr Alison Birtle**	Clinical Oncologist	Preston
Professor Robert Huddart (Outgoing Chair)	Clinical Oncologist	London
Dr Ashok Nikapota	Clinical Oncologist	Brighton
Mr Andrew Winterbottom	Consumer	High Wycombe
Dr Sally Appleyard*	Specialist Registrar Clinical Oncology	Sussex
Professor Emma Hall	Statistician	London
Professor James Catto	Surgeon	Sheffield
Mr Mark Johnson (Deputy Chair)	Surgeon	Newcastle
Mr Param Mariappan (Incoming Chair)	Surgeon	Edinburgh
Dr Rik Bryan	Urologist	Birmingham
Miss Alexandra Colquhoun	Urologist	Cambridge

* denotes trainee member

**denotes non-core member

Appendix 2

CSG & Subgroup Strategies

A – Main CSG Strategy

The main CSG strategy remains to offer as broad a research portfolio as possible, ideally to develop a high quality competitive trial suitable for every patient. This requires a combination of pragmatic trials allowing smaller units to actively participate in bladder and renal trials, balanced with more complex interventional studies.

To do this, an optimal skill mix is required on the CSG and to succession plan. Whilst the CSG membership and that of the Subgroups has been refreshed, it is important to highlight that the pool of research active clinicians in these tumour types is significantly smaller than, e.g. breast cancer, and thus it is important to retain as well as refresh membership, particularly where members continue to make a significant contribution to the Group and portfolio activities.

Immunotherapies have an increasing role in the management of both bladder and renal cancer and have become a standard of care in both diseases. The CSG membership contains international leaders in this area and the Subgroups aim to use their experience to maximal effect. We therefore aim to continue to develop immunotherapy studies in both diseases that explore novel combinations and clinical settings.

The role of patients as research champions is paramount and both consumers, together with KCSN and FBC, continue to work with the CSG to train patient representatives as research experts to liaise with other patients and to exert pressure on research inactive clinicians. All current portfolio interventional trials collect quality of life data and there are a number of studies with a primary qualitative endpoint to allow us to better inform patients on the optimum choice of radical treatment. The CSG has particularly strong consumer input and there is an opportunity to build upon their already excellent work and to consider opportunities in PROM research.

The use of and challenges in expanding the translational work of the CSG has been highlighted already, with withdrawal of funding from POUT-T prematurely and unsuccessful applications for tissue collection for two other portfolio interventional trials. Given the already successful work from LAMB in informing the biomarker directed Rucaparib and Enzalutamide arms of ATLANTIS, the CSG will need to consider other funding sources to continue this component of its portfolio. NAXIVA and A-PREDICT both have rich translational components and information from these studies will inform the development of future studies. TRACERx Renal is an Internationally leading translational research programme resulting in several high impact publications this annum in RCC. The CSG will use the experience gained from TRACERx to instruct high quality translational research in other studies across both diseases.

Several years ago, the Bladder CSG conducted a national audit of surgical barriers on recruitment into bladder trials and has attempted to act on the feedback. One key message to develop pragmatic trials deliverable in smaller units has been rectified, yet some CRNs and urologists continue to fail to engage. Working with the SSLs, together with a direct approach from the CSG Co Chairs and BAUS Oncology, the Group will continue to try to overcome this issue. The work of the Surgical Subgroup directly addresses the barriers to engagement of the renal surgical community and it is of strategic importance to us that this issue is addressed.

There is an unmet need for patients with node positive bladder cancer; previous attempts to design a study for this patient group have been unsuccessful but there is now momentum to achieve this. In addition, the interface between systemic therapies and radiotherapy has been identified as a key research area.

B – Advanced Bladder Cancer Subgroup Strategy

The Subgroup strategy works towards our central objective to 'increase cure rates by improving systemic therapy as a component of multimodality therapy' in the following ways:

- Optimising systemic therapy by developing new drug hypotheses to test in MIBC
    - Efficient delivery of proof of concept studies in advanced disease exemplified by the development of the ATLANTIS precision medicine platform in the maintenance therapy setting.
    - Working towards options for practice changing trials of neoadjuvant therapy through initiation of studies in this clinical setting. Current examples of recruiting trials include NeoBLADE, ABACUS and SPIRE.
    - Working in collaboration with industry to deliver high quality trials of novel agents in areas of unmet need. In addition to the multiple examples on which we have recently published (e.g., LaMB, PLUTO), current examples of trials in recruitment include ATLANTIS, SPIRE, ABACUS, NeoBLADE. We have further emerging trials in development involving collaborations with pharma partners
- Delivery of potentially practice changing studies
    - Implementing POUT, the first ever randomised phase III trial of adjuvant therapy in upper tract TCC, and development of a successor study POUT 2.
- Development of a larger translational research programme
    - Utilisation of the LaMB and ATLANTIS sample sets to allow generation of data on biomarker rates to facilitate new hypotheses to include in the latter trial.
    - Entry of bladder cancer patients into the 100,000 Genomes Project and going forward to begin analyses of data emerging from this project.
    - Coordination of a collaborative approach to utilisation of samples sets from the Subgroup's prior and ongoing studies.

C – Penile Subgroup Strategy

The Penile Subgroup strategy is to:

- Hold regular six monthly meetings with the opportunity of joining in person or by teleconference.
- Provide opportunities for advice and support of applications for grants.
- Increase engagement in clinical trials through promotion of clinical trials and regular engagement with supraregional teams.
- Regularly review Subgroup membership and widening of the membership base to increase contribution to future trials development.
- Ensure consumer involvement in all projects.
- Ensure trainee involvement in the Subgroup to promote development of future researchers.

D – Surgical Subgroup Strategy

The Surgical Subgroup strategy is:

- Regular teleconference meetings every 3 months to facilitate rapid development of trial ideas to design and delivery.
- Involvement of each member of the Subgroup with a specific study within our portfolio.
- Use the Subgroup as a proving ground for members of the main CSG and also new trial CIs. Invitation of selected subgroup members to the main CSG to consider applying for membership.
- Engagement with BAUS Oncology and BAUS academic section on promotion of new trials at their meetings and newsletters.
- Regular review of Subgroup membership to ensure all members are contributing.
- Ensure strong background information (literature review, BAUS database analysis, canvassing urologist opinion) before new trial plans developed more formally.
- Delivery and completion of feasibility studies in contentious areas to prove recruitment can be achieved, i.e. NAXIVA in IVC tumour thrombus, NEST- RCT of ablation vs surgery for SRMs.
- Close liaison with oncologists for neoadjuvant and adjuvant trials, with greater engagement of urologists in the TDG/TMG of these studies and also providing information to the urological community during development phase.

- Embedding translational research as much as possible, urologists are well placed to deliver on this as demonstrated in the past (A-PREDICT, NAXIVA, TRACERx Renal, SCOTRRCC).

E – T2 & Below Subgroup Strategy

The Subgroup aims to develop and support studies aiming to enhance the care of patients with non-metastatic bladder cancer. We will seek to improve the patient experience through

enhancing cancer control and maximising quality of life. Key targets areas of the Subgroup include:

- To enhance the outcomes of patients with high risk NMIBC through
    - Improved diagnostics utilising developments and knowledge in genomics and gene profiling.
    - Optimised adjuvant therapies both intravesical and systemic.
    - Exploration of the optimal approach to the use of radical surgery.
- To develop improved bladder sparing approaches in muscle invasive bladder disease.
- To work with the Systemic Treatments Renal Cancer Working Party Strategy to improve neo-adjuvant, concomitant and adjuvant therapies for patients with MIBC.
- To seek to understand better, and then improve, factors that impact on patient quality of life and experience of bladder cancer treatment.

We will seek to achieve these goals by utilising improved knowledge of tumour biology from translational research projects and through advances in drug development leading to enhanced treatment personalisation.

F – Systemic Treatments Subgroup

The newly formed RCC systemic treatment subgroup aims to generate internationally competitive interventional studies across all stages of the disease by:

- Having a talented ambitious group membership consisting of experienced and lesser experienced investigators in a supportive and co-operative environment.
- Having an explicit expectation that all members take ownership for developing at least one study whilst on the group
- Monthly teleconference meetings. This frequency was found to be necessary in the development of the PRISM and TRIBE studies
- Using pharma contacts of experienced group members to bring investigational products to the group.

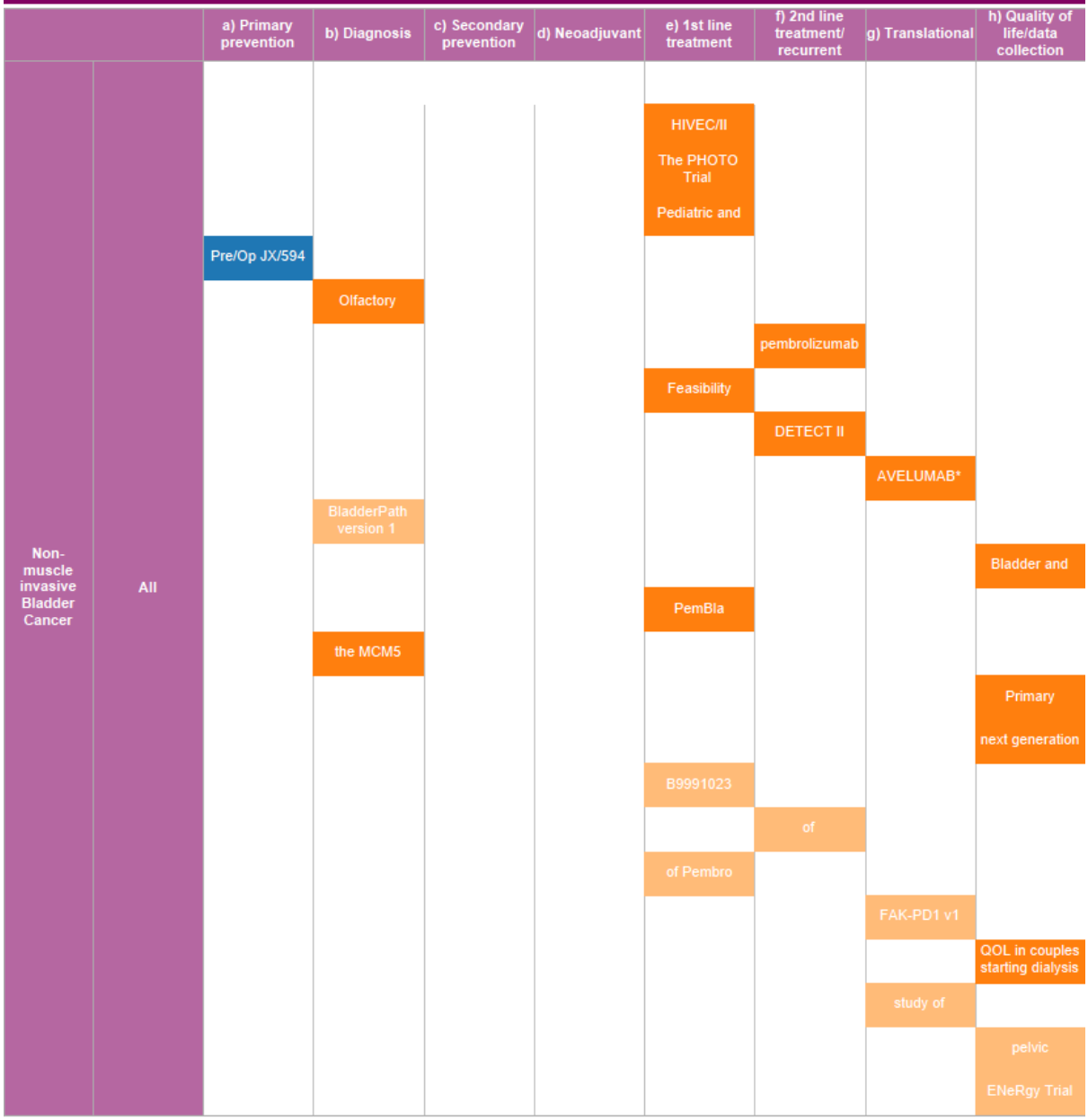
Appendix 3

NCRI portfolio maps

Bladder and Renal Cancer

Map A – Bladder Non-muscle invasive

Click ↓ below to reset map



Filters Used:
Active Status: All, **CSG Involvement**: All, **Funding Type**: All, **Phase**: All, **LCRN**: None

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NCRI National Cancer Research Institute

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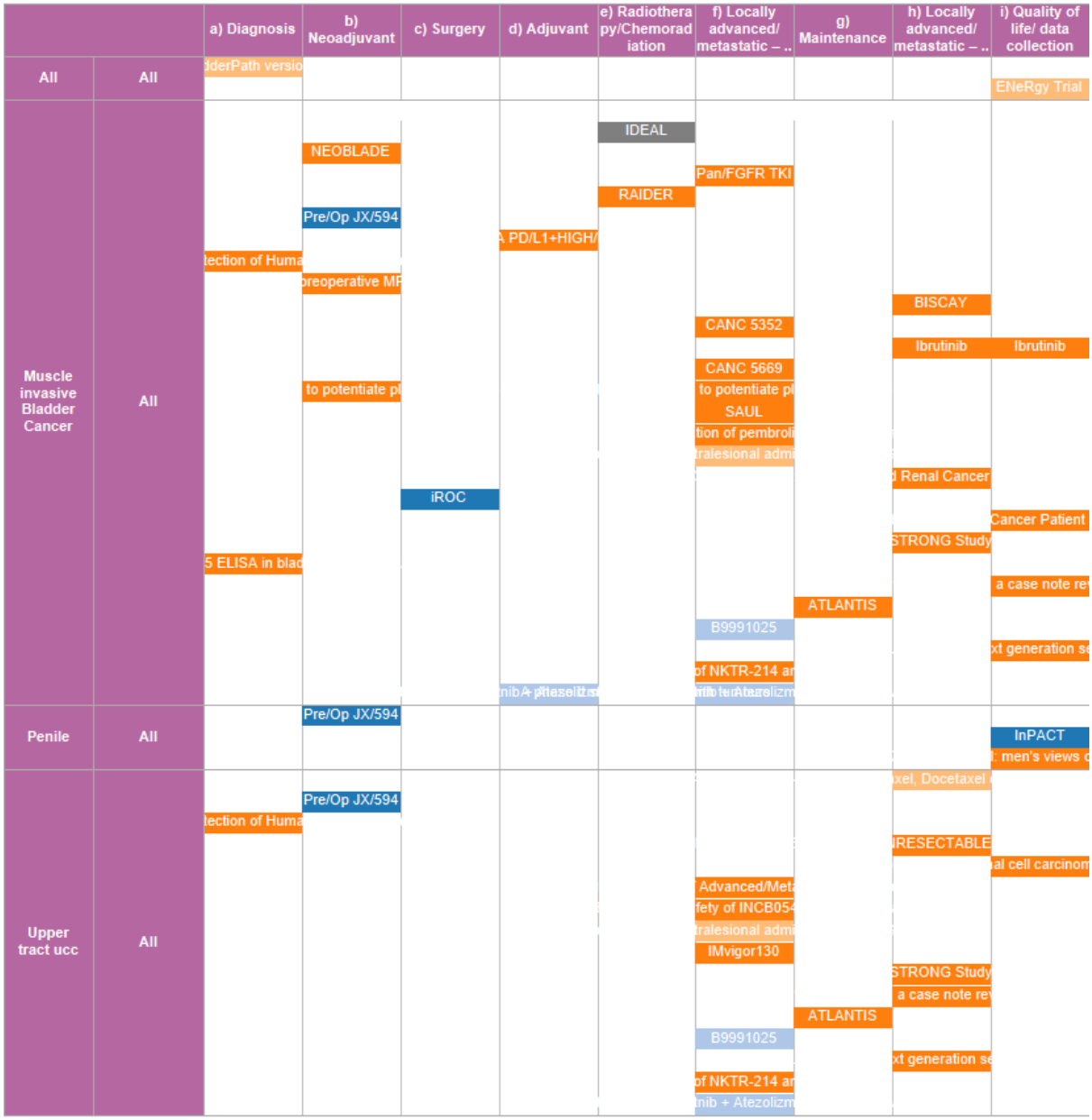
NCRI portfolio maps

Bladder and Renal Cancer

Map B – Bladder Muscle invasive, urothelial cell carcinoma, penile

Click ↓ below to reset map



Filters Used:
Active Status: All, **CSG Involvement**: All, **Funding Type**: All, **Phase**: All, **LCRN**: None

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NCRI portfolio maps

Bladder and Renal Cancer

Map C – Renal clear cell, non-clear cell, adrenal

Click ↓ below to reset map

		a) Neoadjuvant	b) Surgery	c) Adjuvant	d) 1st line metastatic	e) 2nd line metastatic	f) 3rd line metastatic	g) Non-interventional
Adrenal	All							
Clear cell	All	NAXIVA	Pre/Op JX/594 assisted partial nep	IMmotion010 l-Adjuvant MK-3475	combined with Ipilim NIB IN PREVIOUS CALYPSO IM/201 HERAPIES IN PATI Carcinoma after che in RCC; Immune Bi 2 of NKTR-214 and PRISM Trial b PASS Study-F-FR	MLN0128		Genetics of Pap SCOTRRCC DETECT II
Non-clear cell	All	The REMAP study			o (Sutentr) Monothe KEYNOTE-426 Keynote/427 80-G000-307 (CLE	E7080 plus Everoli		SCOTRRCC TRACERx Renal
Other	All			ab in Patients with R	CANC 5334 TITAN RCC CHECKMATE 9ER olizumab open label			ANC - 3263 ADONI al Cancer Patient Re Tumouroids 001 Tissue Researc

Filters Used:
Active Status: All, **CSG Involvement**: All, **Funding Type**: All, **Phase**: All, **LCRN**: None

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NCRI National Cancer Research Institute

Designed and maintained by **NCRI Clinical Research Groups (CRGs)** & **NIHR**

Appendix 4

Top 5 publications in the reporting year

Please note that this section was not completed

Trial name & publication reference	Impact of the trial	CSG involvement in the trial
1. Randomized Phase II Study Investigating Pazopanib Versus Weekly Paclitaxel in Relapsed or Progressive Urothelial Cancer. Jones RJ et al, J Clin Oncol. 2017 Jun 1;35(16):1770-1777	First randomised and cohesive data on standard arm as well as well as for experimental arm.	Developed by CSG
2. Phase III, Double-Blind, Randomized Trial That Compared Maintenance Lapatinib Versus Placebo After First-Line Chemotherapy in Patients With Human Epidermal Growth Factor Receptor 1/2-Positive Metastatic Bladder Cancer. Powels2017. J Clin Oncol. 35(1):48-55	First ever maintenance therapy in bladder cancer. Huge biorepository which has informed the current ATLANTIS trial among others regarding patient selection.	Developed by CSG
3. COAST (Cisplatin ototoxicity attenuated by aspirin trial): A phase II double-blind, randomised controlled trial to establish if aspirin reduces cisplatin induced hearing-loss. Crabb SJ et al, Eur J Cancer. 2017 Dec; 87:75-83.		Developed by CSG

Appendix 5

Recruitment to the NIHR portfolio in the reporting year

In the Bladder & Renal CSG portfolio, 29 trials closed to recruitment and 33 opened.

Summary of patient recruitment by Interventional/Non-interventional

Bladder

Year	All participants		Cancer patients only		% of cancer patients relative to incidence	
	Non-interventional	Interventional	Non-interventional	Interventional	Non-interventional	Interventional
2013/2014	648	287	648	287	6.2	2.7
2014/2015	69	262	69	262	0.7	2.5
2015/2016	763	604	649	604	6.20	5.77
2016/2017	5827	948	5624	948	53.70	9.05
2017/2018	3351	1176	3311	1166	31.61	11.13

Renal

Year	All participants		Cancer patients only		% of cancer patients relative to incidence	
	Non-interventional	Interventional	Non-interventional	Interventional	Non-interventional	Interventional
2013/2014	596	345	497	322	6.1	4.0
2014/2015	154	255	130	255	1.6	3.1
2015/2016	61	399	61	378	0.75	4.64
2016/2017	148	315	148	315	1.82	3.87
2017/2018	170	323	170	318	2.09	3.91